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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/454,737	12/06/1999	MICHEL PERRICAUDET	8076.85USC1	4183

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EXAMINER	
GUZO, DAVID	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/454,737	Applicant(s) PERRICAUDET ET AL.	
	Examiner Gerald G Leffers Jr.	Art Unit 1636	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,17-19 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17-19 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 15, 18-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perricaudet et al. on view of Quantin et al., Rice et al. and further in view of Ordahl et al.

This rejection is maintained for reasons of record in the previous Office Action (Paper #22) and for reasons outlined below. The rejection is expanded to include claim 22 as a result of applicants' amendment filed 7/17/02.

Applicants traverse this rejection by asserting that Perricaudet et al. does not teach that another promoter (other than the adenoviral major late promoter, MLP) can be used in adenoviral vector constructs and there is no indication what promoter was used to express beta-galactosidase in mouse muscle tissues *in vivo*. Applicants assert that there is no teaching in Perricaudet et al. that by using the adenoviral vector, the polypeptide of interest is expressed in muscle cells and is distributed throughout the muscle mass and that there is no teaching that the adenoviral vector can be expressed in cardiac muscle cells. With regard to the Quantin et al. reference, applicants

assert that there is no teaching that cardiac muscle can be infected using the adenoviral vector and that the polypeptide is distributed throughout the muscle mass. With regard to the Rice et al. reference applicants assert that the use of E1-deleted adenoviral vectors comprising the RSV LTR fused to a CAT gene to express the protein in HeLa cells cannot be equated with expression in muscle cells. With regard to the Ordahl et al., applicants assert that there is no disclosure of an adenoviral vector and that the teachings of Ordahl et al. relate to use of a plasmid pRAVcat as a reporter plasmid. Furthermore, applicants assert that Ordahl et al. use different methods of treatment of cardiac and skeletal muscle cells *in vitro* and that the results of Ordahl et al. cannot be compared to those using the claimed adenoviral vectors. Applicants assert that there is no evidence that the claimed defective adenoviral vectors could penetrate the sheath surrounding the muscle mass and be distributed throughout the muscle mass.

Applicants arguments filed 7/17/02 have been considered but are not persuasive. First, it is noted that applicants' arguments are often directed against individual references in isolation with applicants subsequently concluding that the individual reference does not teach the entire invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). With regard to Perricaudet et al.

not teaching use of other promoters, it is noted that Perricaudet et al. is a review article, and cites references which disclose use of other promoters to drive expression of genes in recombinant adenoviral vectors. For example on page 57, Perricaudet et al. recites the data generated by Bailey et al. (1985) wherein the adenoviral vector comprised the E1a promoter operably linked to the sequence encoding HbsAg. Second, with regard to the specific promoter used to drive expression of the beta-galactosidase in muscle cells, the examiner, in the previous office action admits that Perricaudet et al does not disclose use of the claimed RSV promoter to drive expression of the gene of interest in adenoviral vectors. With regard to applicants assertions that neither Perricaudet et al. nor the other references teach that the adenoviral vector can be expressed in cardiac muscle cells, the examiner notes that none of the claims is limited to an adenoviral vector capable of expressing proteins in cardiac muscle cells. The claims merely recite adenoviral vectors capable of expressing proteins generically in **muscle cells**.

With regard to applicants assertion that none of the cited references teach that by using an adenoviral vector the polypeptide of interest is expressed throughout the muscle mass, this does not appear to be a structural limitation on the claimed adenoviral vector compositions. Rather, the ability of the vector to be evenly distributed throughout the muscle mass is more a property of the methodology by which the vector is administered to the host. Since the instant claims are not method claims, but instead are composition claims, the obviousness of the claimed vectors

must be decided by the structure of the claimed vector, not by how the vector composition can be subsequently used to deliver a gene of interest to muscle tissue. With regard to the teachings of the Quantin et al. reference, applicants' assertion that Quantin et al. does not provide a teaching that the adenoviral vector can express a polynucleotide in cardiac muscle cells is confusing because this is not a limitation recited in the claims. With regard to the teachings of Rice et al., applicants do not deny that the reference teaches an E1-deleted adenoviral vector comprising the RSV LTR promoter operably linked to the gene of interest. The examiner has used this reference to show that the RSV LTR promoter has been used to drive expression of a gene of interest in adenoviral vectors. Instead, applicants have analyzed the reference in isolation and indicate that the reference does not disclose whether the RSV LTR can be used to drive expression of polynucleotides in muscle cells and does not disclose expression of polynucleotides throughout the muscle mass. The examiner again notes that the Rice et al. reference is not applied to supply the teachings which applicants assert are missing from the reference. With regard to the teachings of Ordahl et al., the examiner again notes that applicants have analyzed the reference in isolation and assert that because it does not teach the entire invention, it cannot be used to render the invention obvious. Given the above analysis of applicants' arguments, it must be considered that the claimed invention is *prima facie* obvious over the combination of the cited references.

3. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Perricaudet et al. in view of Rice et al. and Ordahl et al. and further in view of Nabel et al.

This rejection is maintained for reasons of record in the previous Office Action and for reasons outlined below.

Applicants traverse this rejection by asserting that Nabel et al. teaches many embodiments and "...that it is only logical that the many specificities disclosed under each embodiment cannot be freely exchanged, but are specific to certain embodiments disclosed under the very specific headings in Nabel et al." (Applicants arguments, p. 6).

In response, the examiner notes that applicants present no evidence that the skilled artisan, given the teachings of Nabel et al. that viral vectors such as adenoviral vectors (which are a well characterized and widely used viral vector system) can be used to deliver and express specific genes with thrombolytic properties in cells such as muscle cells, would not have been motivated to use adenoviral vectors to express genes having thrombolytic properties, especially given the teachings other references cited in the rejection.

Applicants assert that the skilled artisan would not come to the conclusion that an adenoviral vector could be used to express a gene with thrombolytic properties in muscle cells because Nabel et al. does not provide an actual demonstration of such activity.

In response, the examiner notes that applicants are again analyzing each reference in isolation.

The remaining references teach generation of E1-deleted adenoviral vectors to express genes of interest in muscle cells and that Nabel et al. merely teaches that adenoviral vectors can also be used to express genes with thrombolytic properties in cells such as smooth muscle cells.

Applicants analyze the Nabel et al. reference with regard to the techniques used (i.e. use of high pressure catheters) to deliver the recombinant viral vectors to target tissue or cells and indicate that Nabel et al. does not teach delivery of adenoviral vectors to muscle cells by any technique. Furthermore, applicants indicate that the only section of Nabel et al. which refers to thrombolytic proteins involves the use of cells transformed with the vector, not the vector alone, to treat diseases.

In response, the examiner notes that focusing on the methods by which the vectors are delivered to target cells is, in this case, not germane to the instant adenoviral vector composition claims. The facts are that Nabel et al. recites the use of adenoviral vectors (among a small list of viral vectors) to deliver genes of interest (which can be genes encoding proteins with thrombolytic properties) to cells *in vitro* or *in vivo*. The target cells can be muscle cells. Furthermore, applicants' assertion that Nabel et al. teaches use of cells infected or transformed with viral vectors encoding thrombolytic agents is not germane again because the methods by which the claimed vectors may subsequently be used is not relevant to vector composition itself. Given the above analysis of applicants' arguments, it must be considered that the claimed

invention is *prima facie* obvious over the cited art.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15, 17-19 and 21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,099,831. Although

the conflicting claims are not identical, they are not patentably distinct from each other because of reasons of record in the previous Office Action (Paper #22). Claim 21 has been added to this rejection as a result of applicants amendment filed 7/17/02 and is covered by the rejection made in the previous Office Action.

Applicants respond to this rejection by indicating that the rejection be held in abeyance until there is allowable subject matter. Applicants indicate that they will file a Terminal Disclaimer at that time. The rejection will therefore be maintained.

Any rejections not repeated in this Office Action are withdrawn.

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
October 19, 2002

DAVID GUZO
PRIMARY EXAMINER